Outcomes in Oncology

Ochsner Cancer Institute's Report to Physicians
April 2014

ochsner.org/cancer

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Treatment Advances in Pancreatic Cancer

Dear Physicians,
In this inaugural issue of Ochsner Cancer Institute's "Outcomes in Oncology" newsletter, Dr. Charles Conway, surgical oncologist and pancreatic surgical specialist, gives us insight into the hazards of pancreatic cancer and the advanced diagnostic and therapeutic options available today.

The purpose of this "Outcomes in Oncology" newsletter series will be to provide the healthcare professionals of the Gulf South with a timely and accurate assessment of important cancer problems that they may encounter in their day to day practice.

Dr. Conway and the clinical team at the Ochsner Cancer Institute have established an outstanding opportunity for the pancreatic cancer patient to benefit from the expertise of their multidisciplinary treatment group of gastroenterologists, pancreatic surgeons, radiation oncologists, medical oncologists and nurse specialists.

Advanced minimally invasive laparoscopic and robotic surgical approaches to pancreatic cancer resection have been championed by Dr. Conway's surgical team. Their surgical experience is the largest in the Louisiana and Mississippi Gulf South and their surgical outcomes have been outstanding.

The survival of patients treated by this outstanding, dedicated group of health professionals rates well above the national average.

Thank you for participating this important educational effort provided by the Ochsner Cancer Institute.

Sincerely,

Rodney J. Landreneau, M.D.
Medical Director, Ochsner Cancer Institute

Ochsner™ Health System

Recent Trends in the Treatment of Pancreatic Cancer

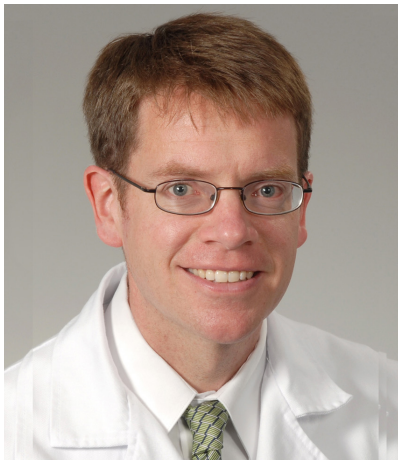
By W. Charles Conway II, M.D.
Surgical Oncology

Background

Pancreatic cancer continues to be one of the deadliest forms of malignancy. Estimates for 2013 include 45,220 new cases and 36,460 deaths. (1) To put this in perspective, there are 234,580 new breast cancer cases and 40,030 deaths (1). Overall, pancreatic cancer is the 4th leading cause of cancer death in the U.S. Most patients present with vague symptoms of abdominal pain, weight loss and fatigue. Other findings that more precisely direct a pancreatic evaluation are jaundice, dark urine, new onset diabetes and an episode of pancreatitis. Although there has not been a great deal of optimism about the treatment of this disease in the medical community, there are glimmers of hope. Current five-year survival after surgical resection is approximately 25 percent (3,4) and newer chemotherapy agents are finally showing significant response rates—up to 32 percent—unheard of in the gemcitabine era (4). Current staging is based on the 7th edition of the American Joint Committee on Cancer (AJCC) manual.

Patient Evaluation

Cross-sectional imaging is used most commonly during the evaluation of patients with a pancreatic mass and should include a computed tomography (CT) scan or magnetic resonance imaging (MRI) with a dedicated pancreas protocol (5). Endoscopic ultrasound (EUS) is extremely useful and can provide a tissue biopsy, necessary when considering neoadjuvant treatment, a practice that is becoming increasingly common. Positron emission tomography (PET) scanning is still considered investigational by the National Comprehensive Cancer Network (NCCN.gov) and is currently employed selectively. Multidisciplinary treatment planning is vital and has been shown to alter treatment strategy in 24 percent of cases. (6) Like all cancers, treatment for this disease needs to be patient based, not physician specialty driven.



W. Charles Conway II, M.D.

Surgical Selection

In patients without metastatic disease and good performance status (ECOG 0-1), potentially curative surgical resection is considered. After many years of various meanings of "resectable," we now have consensus definitions (5). They are essentially driven by the relationship of the tumor to local blood vessels including the portal vein (PV), superior mesenteric vein (SMV), hepatic artery (HA), celiac axis (CA) and superior mesenteric artery (SMA) (Figure 1). If the tumor is not touching any of the vessels, it is considered, "resectable," and often offered immediate surgery (Figure 2).

If it is involving the SMV/PV, HA, or abutting (<180° interface) the SMA, it is considered, "borderline resectable." Although these tumors are technically resectable, and we have the ability to reconstruct each one of these vessels, this group of patients has a higher risk of harboring early, initially undetected metastatic disease, are at risk for a margin-positive resection (7) and for these reasons, are most often treated with a neoadjuvant approach. Our current regimen for this scenario includes four cycles of FOLFIRINOX followed by 5-FU chemoradiation. This is the treatment used in the multi-center clinical trial sponsored by the Alliance group (A021101) that is currently open at Ochsner. (clinicaltrials.gov) If the patients have not progressed (and hopefully shown some response) on repeat imaging after the neoadjuvant treatment, they are offered surgery. Survival in this group that completes neoadjuvant treatment and surgery is reported to be as high as 36 percent at five years (3), which may improve further with newer agents. We have seen significant radiographic responses utilizing the Alliance regimen. (Figure 3) With improved systemic agents, neoadjuvant strategies may soon be employed for all surgical candidates.

Surgical Outcomes

The most commonly performed surgical procedure for pancreatic cancer is a pancreaticoduodenectomy, or the Whipple procedure. Distal pancreatectomy and total pancreatectomy are done less often. There was a time when this operation was considered prohibitively dangerous, but in the modern era, it can be done with low mortality (8). A recent review of this procedure at Ochsner, the highest volume pancreas program in Louisiana, revealed an average of 40 Whipple procedures per year, fewer than 2 percent mortality (risk adjusted mortality index 0.43) and a complication index of 0.79 (pancreatic leak rate is 7 percent). It is clear in the literature that surgeons are good at what they do often and these outcomes come with experience. Similar to esophagectomy, the Whipple procedure is a complex operation that has a mortality rate directly correlated to the institutional procedural volume. 9, (Figure 4) Outcomes have also been shown

to improve with the institution of comprehensive peri-operative pathways (10). We recently instituted such an algorithm and noted a reduction in average length of stay from 14 to 8 days ($p<0.05$). This pathway is truly comprehensive, outlining the initial work-up, pre-operative optimization, intra-operative anesthetic management and a detailed post-operative plan that includes significant patient participation and empowerment. Similar to other areas of surgery, minimally invasive (MIS) approaches to pancreatic surgery have been developed in hopes of reducing the morbidity related to wounds and hasten recovery. This has most often been applied to distal pancreatectomy with excellent results, but also the Whipple procedure. (11) Although there is not yet a tremendous amount of data, early results of MIS Whipple appear promising. At Ochsner, we currently perform the majority of distal pancreatectomies in a MIS fashion, with the surgical robot. We also recently performed the first totally robotic Whipple in Louisiana.

On the opposite end of the spectrum, vascular resection and reconstruction can be done safely during the Whipple procedure (12). High volume pancreatic surgeons can perform en bloc vascular removal to ensure margin-negative resections (Figure 5). At Ochsner, we resect and reconstruct the SMV/PV in 30 percent of our Whipple procedures. Less commonly, we remove and rebuild the HA when necessary, and at times the CA for body tumors.
All of these patients are well selected with neoadjuvant treatment to ensure these aggressive procedures are not performed on patients with early metastatic disease.

> "Although there has not been a great deal of optimism about the treatment of this disease in the medical community, there are glimmers of hope."

Chemotherapy

As mentioned above, there are recent signs that current chemotherapy regimens are significantly more effective than those used previously. In the metastatic setting, FOLFIRINOX increased median survival to 11 months, compared to 7 months for Gemcitabine. (4) Response rates for this regimen were 30 percent overall. This regimen is being incorporated into neoadjuvant schemas, and we are seeing significant radiographic and pathologic responses during treatment. Whether this will equate with improved survival in this setting is not yet known. The other recently reported regimen is Gemcitabine plus Abraxane (nab-paclitaxel). This combination was shown to improve survival over Gemcitabine alone with a 23 percent overall response rate in the metastatic setting. (13) This regimen will be part of an upcoming multicenter adjuvant trial.

> "Current 5-year survival after surgical resection is approximately 25% and newer chemotherapy agents are finally showing significant response rates, unheard of in the Gemcitabine era."

Closing

Pancreatic cancer continues to be extremely difficult to treat. There are glimmers of hope, however. Modern surgical techniques can safely remove early tumors, and we are finally seeing improvement in the systemic therapies. Dedicated clinical teams, focused on these patients, and a renewed emphasis on funding pancreatic cancer research will continue to foster progress in treating this disease. (Figure 6) We have reason for optimism.

To refer a patient, please call the Surgical Oncology Clinic at **504-842-4070**. For 24/7 phone consults and/or patient transfers, please call the Regional Referral Center at **1-855-OHS-LINK (647-5465)**.

For more information, please visit **ochsner.org/cancer**

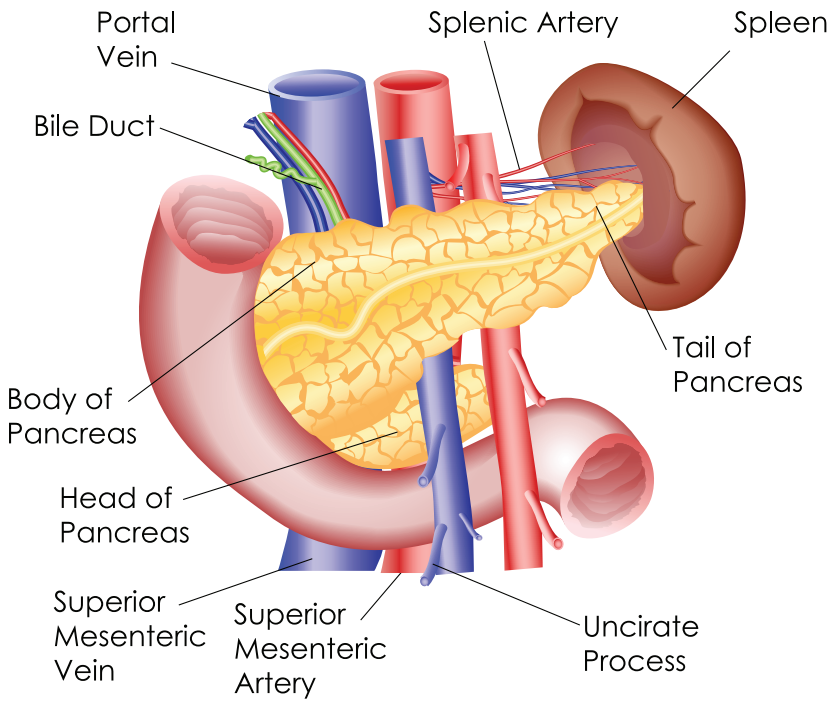


Figure 1 – Medical illustration of pancreas.

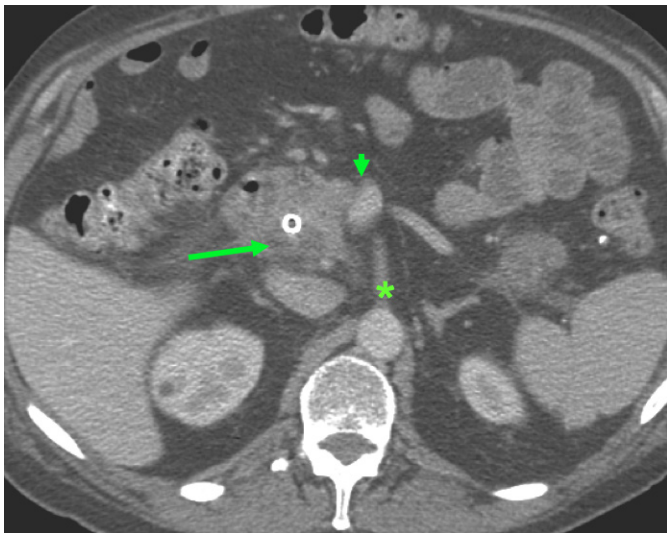


Figure 2 – In this figure, the CT scan indicates a pancreatic mass (arrow) that would be considered, "resectable." The SMV (arrowhead) and SMA (asterisk) are widely free from the tumor.

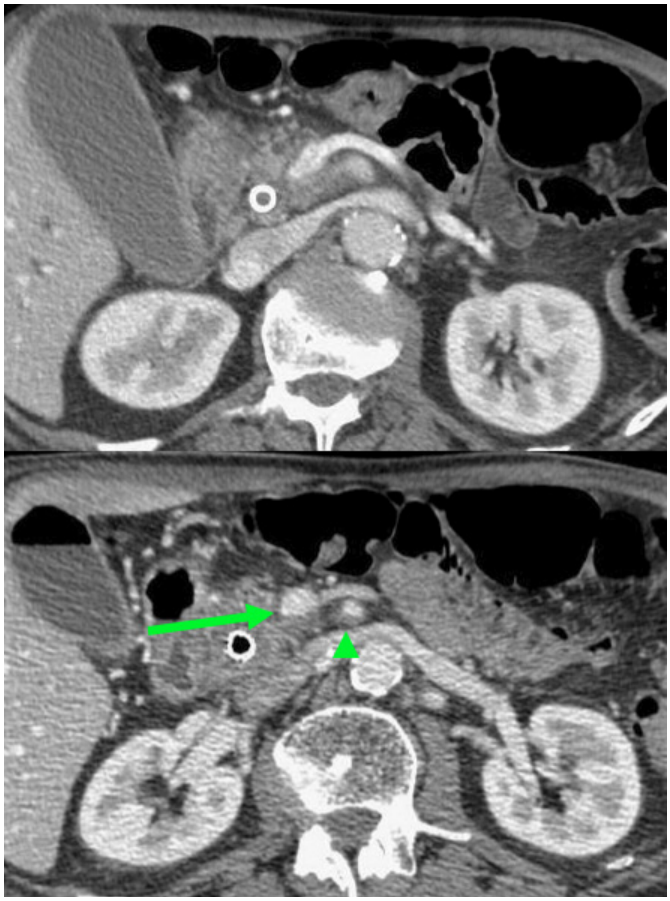


Figure 3 – Depicted here is a patient who received pre-operative FOLFIRINOX. The top image is pre-chemotherapy and shows significant SMV and SMA involvement. The bottom image, after chemotherapy and radiation, indicates reduced SMA involvement (arrowhead), and a widened caliber of the SMV (arrow). This patient's CA 19-9 was initially 151 and went to 19 after neoadjuvant treatment.

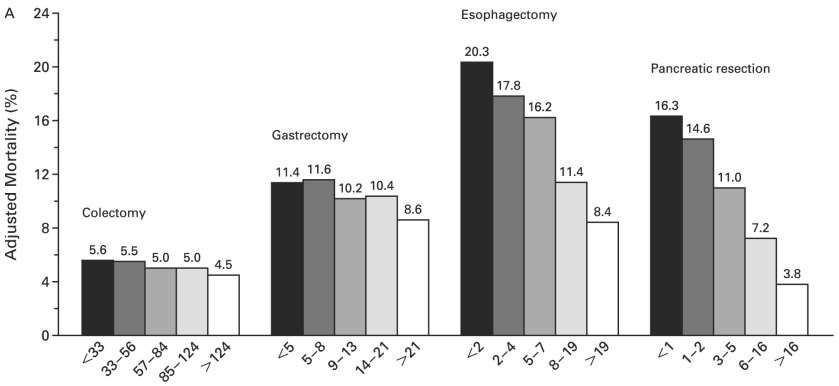


Figure 4 – This graph, reprinted with permission, shows mortality as it relates to hospital procedure volume. For complex operations, including esophagectomy and pancreaticoduodenectomy (Whipple), there is a direct relationship with higher volume institutions having the lowest procedure-related mortality. Reproduced with permission from Hospital Volume and Surgical Mortality in the United States. New England Journal of Medicine. 2002

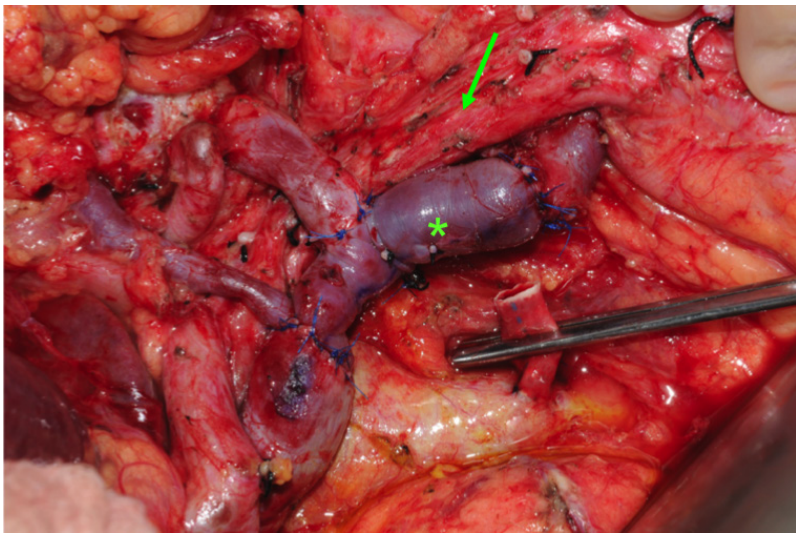


Figure 5 – Depicted here is a photograph that shows a reconstructed SMV/PV (asterisk) and the skeletonized SMA (arrow). This cases required a temporary mesocaval shunt to perform the venous reconstruction (clamp).

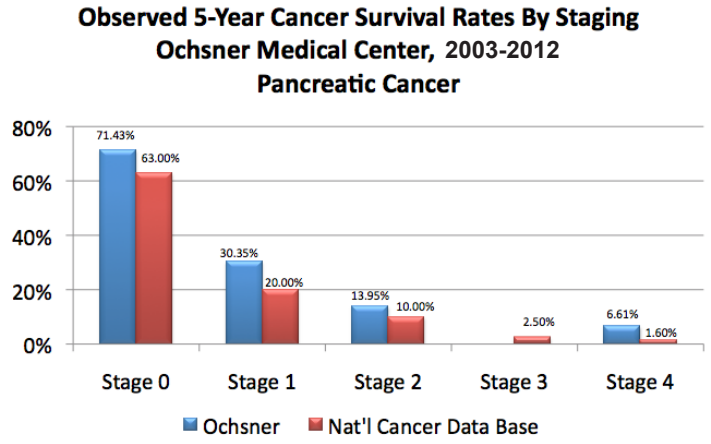


Figure 6 – This graph indicates survival of patients with pancreatic cancer treated at Ochsner, grouped by stage, compared with all patients with this disease in the National Cancer Data Base. Ochsner Medical Center, Adults Cancer Patients (18 years +) , 2003 – 2012. Ochsner N: Stage 0 = 5; stage 1 = 317 Stage 2 = 103; Stage 3 = 415; Stage 4 = 606. National Cancer Data Base (NCDB) American College of Surgeons Commission on Cancer, 2003 – 2006.

Continuing Medical Education Questions

1 – Which of these statements regarding pancreatic cancer is false?

A. Pancreatic cancer is the 4th leading cause of cancer death in the U.S.
B. There are nearly as many deaths in the U.S. each year from pancreatic cancer as there are from breast cancer.
C. Survival after surgery for pancreatic cancer is no better than systemic treatment.
D. Current staging of pancreatic cancer relies on the AJCC 7th edition manual.

2 – Which of these statements regarding surgery for pancreatic cancer is true?

A. Outcomes are best in high volume centers.
B. Vascular resection can be done safely with similar outcomes to patients not requiring vessel removal and reconstruction.
C. Outcomes are best when patients are selected for surgery by a multidisciplinary team and evidence-based paeri-operative pathways are implemented.
D. Minimally invasive surgical techniques can be used safely for pancreatic resection.
E. All of the above.

3 - Which of these statements regarding chemotherapy for pancreatic cancer is false?

A. Chemotherapy is often given pre-operatively for patients with borderline resectable disease, and may become standard for all surgical patients.
B. Current multi-drug regimens have response rates greater than 30 percent.
D. Modern era chemotherapy regimens are no better than Gemcitabine.
E. FOLFIRINOX and Gemcitabine plus Abraxane are associated with improved survival over Gemcitabine alone in the metastatic setting.

Accreditation
The Ochsner Clinic Foundation is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Designation
The Ochsner Clinic Foundation designates this enduring material for a maximum of 1 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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Answers to Continuing Medical Education Questions: 1) C, 2) E, 3) D

Ochsner Health System

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Upcoming CME Oncology Activities:

May 9-10, 2014
33rd Annual Dr. John C Weed OB/GYN Women's Health Symposia
Hotel Monteleone, New Orleans, Louisiana

May 20, 2014
11th Annual Research Day
Brent House Atrium, New Orleans, LA

June 5-8, 2014
12th Annual New Orleans Aeroallergen Conference
Brent House Conference Center, New Orleans, LA

June 12-15, 2014
Gulf States Hospital Society Conference
Grand Marriott, Point Clear, AL

June 27, 2014
Pulmonary Hypertension Conference
Brent House Conference Center, New Orleans, LA

Information and registration for all conferences are available on our website, ochsner.org/cme

Upcoming "Outcomes in Oncology" Topics:

May: Head/Neck Surgical Oncology
June: Urologic Oncology
July: Dermatologic Oncology
August: Colorectal Oncology
September: Hematologic Malignancy
October: Breast Cancer
November: Gynecologic Oncology
December: Neurooncology

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